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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/711,621	04/17/00	HANG	210121.47005

EXAMINER

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ART UNIT	PAPER NUMBER
1635	10

DATE MAILED: 10/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/551,621	Applicant(s) JIANG ET AL.	
	Examiner Janet L Epps	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-79* is/are pending in the application.

4a) Of the above claim(s) *1-3,13-16,21-38,40-43 and 48-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *4,5,7-12,17-20,44-47 and 77-79* is/are rejected.

7)☐ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group II, claims 4-12, and 17-20, 39, 44-47, and 77-79, drawn to polynucleotides and polynucleotide compositions, and species SEQ ID NO: 474, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the subject matter SEQ ID NO: 463-468 and 474, represent sequences that are related one to the other, since they represent full-length or splice variants of the full-length breast tumor antigen B726P. Furthermore, Applicants argue that a search of SEQ ID NO: 474 will necessarily identify sequences "related" to SEQ ID NO: 463-468. However, since SEQ ID NO: 474 is structurally different from SEQ ID NO: 463-468, it is unclear how the examiner would be able to identify sequences related to SEQ ID NO: 463-468 by means of doing a search of SEQ ID NO: 474.

Moreover, Applicants submit that a search of SEQ ID NO: 463-468 and 474 would not constitute an undue search burden on the Examiner to search each of these sequences for a single patent application. This is not found persuasive because although the sequences show some relationship, nevertheless the inventions according to SEQ ID NO: 463-468 and 474 represent structurally distinct nucleotide sequences that encode proteins having different functions and possessing a distinct peptide structure. Additionally, Applicants argue that that 37 CFR 1.141 permits the examiner to examine multiple inventions in a single application without restriction. However, this allowance is based upon the availability of PTO resources. Resources are now stretched to the limit due to the amount of time required to search each sequence against the growing number of sequence databases, so that only one nucleotide sequence should be searched

per application. Therefore, the search of SEQ ID NO: 463-468 and 474 would present an undue search burden on the examiner and on PTO resources.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-3, 13-16, 21-38, 40-43, and 48-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

3. Claims 4-12, and 17-20, 39, 44-47, and 77-79 will be examined to the extent that the instant claims read on the elected sequence of SEQ ID NO: 474. It is also noted that no claim will be allowed which recites non-elected sequences.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: Applicants state that the instant application is a continuation-in-part of US Application 09/389,681, filed on September 2, 1999, which is a continuation-in-part of US Application 09/389,338. This reference is incorrect since application 09/389,681 is a continuation-in-part of US Application 09/339,338.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 4-5, 7-12, 17-20, 39, 44-47, and 77-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 4-5 and 7-12 read on an isolated polynucleotide encoding at least 15 contiguous amino acid residues of a breast tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions, and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in SEQ ID NO: 474. Claim 39 reads on an isolated polynucleotide encoding a fusion protein according to claim 35 that comprises an immunogenic portion of a breast tumor protein or a variant thereof. Claims 77-79 read on an oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a breast tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in SEQ ID NO: 474.

The instant claims read on a broad genus of polynucleotides encoding variants of a breast tumor protein that react with antigen-specific antisera as described above, this genus of polynucleotides encompasses all corresponding sequences from other species, mutated sequences, polymorphic and allelic variants, splice variants, sequences that have an unspecified degree of identity (similarity, homology), and so forth.

Despite knowledge in the art for producing polypeptides that are analogs of a given polypeptide, the specification fails to provide any guidance regarding what specific substitutions, deletions, or insertions of the polynucleotide encoding said polypeptides that are necessary to retain the ability to react with antigen-specific antisera, nor have Applicants provided guidance

as to where allelic or other variants would be expected to be obtained and with the function disclosed.

Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between the genus members are permitted, and neither the specification or the claims provide any guidance as to what specific changes should be made. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is required. Since the disclosure fails to describe the common attributes or characteristics that identify the members of the claimed genus of polynucleotides, and because the genus is highly variant, the disclosed sequence of SEQ ID NO: 474, alone is not sufficient to describe claimed genus.

6. Claims 17-20, and 44-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Inherent in a pharmaceutical composition or an immunogenic (vaccine) composition is the *in vivo* use thereof. The specification contemplates treating breast cancer using immunotherapy comprising the administration of the pharmaceutical or immunogenic compositions comprising the polypeptides of the instant invention. The specification as filed does not provide sufficient guidance or instruction that would enable one of skill in the art to use the claimed compositions throughout the full scope of the claimed invention without undue experimentation. The specification as filed states that the claimed polypeptides were obtained using a PCR-based subtraction using SCID mouse passaged breast tumor RNA. The

specification states that claimed polypeptides were derived from "[g]enes found to be differentially expressed between early and late passage SCID tumor may be stage specific and therefore useful in therapeutic and diagnostic applications." (p. 70 of specification) However, there is no evidence that the claimed polypeptides are specifically expressed in breast tumor cells, or that have they provided a clear comparison between the expression patterns of the claimed polypeptides in normal, un-diseased tissue and breast tumor cells. Applicants clearly have not provided any nexus between the expression patterns of the claimed polypeptides in SCID passaged tumors and the therapeutic efficacy of the claimed polypeptides.

It is not feasible to extrapolate the teachings of the specification to the instant claims since it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable. For example, Gura (Science, 1997, Vol. 278, pp. 1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second paragraph). Due to the known unpredictability of the cancer therapy art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that an isolated polynucleotide comprising SEQ ID NO: 474 could be effectively used in chemotherapy or immunotherapy for treating breast cancer. In addition, Hartwell et al. (Science, 1997, Vol. 278, pp. 1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, however most effective anticancer drugs have been discovered by serendipity and that the exact molecular alterations that provide selective tumor cell killing are unknown and that even

understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (bridging paragraph 1064-1065).

The specification as filed also suggest the use of the pharmaceutical and vaccine compositions recited in the instant claims in a method of gene therapy. However, the specification as filed does not provided sufficient guidelines in this regard. Furthermore, there are many factors that complicate the gene therapy field. According to Anderson (1998), " Gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease. Several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered." (page 30, 5th paragraph).

Moreover, anti-tumor agents must accomplish several tasks to be effective. These agents must be delivered into the circulation that supplies the tumor or metastatic promoter producing cells and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. The specification as filed does not teach one of skill in the art how to deliver the claimed compositions to a particular target tissue within an organism in order to produce a therapeutic result. In addition, variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The claimed formulations may be inactivated *in vivo* before producing a sufficient effect, for example by degradation, immunological activation or due to an inherently short half-life of the formulation. The specification does not provide sufficient guidance or instruction in regard to these issues and provides no working examples that would allow one skilled in the art to use the claimed compositions throughout the full scope of the claims without undue experimentation.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44-47 recite "a polynucleotide according to claim 40." There is insufficient antecedent basis for this limitation in claim 40, since claim 40 recites a "fusion protein according to claim 32." There is no reference to a polynucleotide in claim 40.

Claim Objections

9. Claim 9 is objected to because of the following informalities: Claim 9 recites the phrase "claims claim." It is likely that Applicants have mistakenly duplicated the word "claim." Appropriate correction is required.

10. The elected invention recited in Claim 6 is free of the prior art searched, to the extent that claim 6 is limited to the elected invention according to the polynucleotide comprising the sequence of SEQ ID NO: 474. Although, the polynucleotide sequence of Nordsiek et al. is 20% identical to the overall sequence of SEQ ID NO: 474 of the instant application, and has a best local similarity of 91.1% over 845 nucleotides of SEQ ID NO: 474, the sequence according to Norsiek et al. does not anticipate nor render obvious the full length sequence of SEQ ID NO: 474.

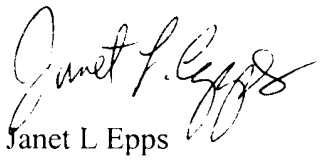
Furthermore, claim 6 is objected to the extent that claim 6 also recites the following non-elected sequences: 2, 4-15, 18-33, 35-47, 49-56, 58, 63-73, 88-116, 141-159, 175, 178, 180, 185, 186, 194, 199, 205, 208, 211, 214-216, 219, 222, 226, 232, 236, 240, 241, 245-246, 252-268,

321-325, 343, 354, 367-369, 377, 382, 385, 389, 395, 397, 400, 408, 411, 413, 414, 416-417, 419-423, 426-427, 429, 431, 435-438, 441, 443-446, 450, 453-454, and 463-468. In order to overcome this objection Applicants are invited to amend claim 6 to remove all reference to the non-elected sequences.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on Mondays through Friday, 9:00AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Janet L Epps
Examiner
Art Unit 1635

jle
October 8, 2001